

# Prognosis of idiopathic cardiomegaly in Jamaica with reference to the coronary arteries and other factors

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*Clinical and epidemiological features of idiopathic cardiomegaly in Jamaica are reviewed, and the high community prevalence of the disorder is shown.*

*The frequent occurrence of sudden or unexpected death in patients whose earlier electrocardiograms had shown repeated ventricular ectopic beats has been noted. Common electrocardiographic findings included a high rate of abnormalities usually regarded as indicative of coronary artery disease: cardiac arrhythmias, particularly multiple ventricular extrasystoles; and high voltage complexes characteristic of left ventricular hypertrophy.*

*The differences and similarities between idiopathic cardiomegaly and coronary heart disease are shown. A possible role for intramuscular lignocaine in the control of the chronic ventricular ectopic rhythms is demonstrated.*

*There is a statistically significant association between idiopathic cardiomegaly and positive serological tests for treponemal infection.*

*The hearts are invariably hypertrophied at necropsy. In some hearts the smaller intramuscular coronary arteries show occlusive changes. Their possible nature and significance are discussed.*

In 1963 we described patients with unexplained cardiomegaly seen clinically and at necropsy at the University Hospital in Jamaica (Stuart and Hayes, 1963). This and subsequent papers showed a high prevalence of the disorder in Jamaica and noted its occurrence in other West Indian communities. The patients were mainly from the lower income groups. In many there was a gradual downhill course with a progressively refractive cardiac failure. In another category the cardiac failure when present was readily controlled and death was either sudden or unexpected. There were also a number of patients in whom cardiac hypertrophy was an unexpected finding on examination for unrelated reasons.

Three clinical types were described, simulating ischaemic heart disease, valvular heart disease, or constrictive pericarditis. At necropsy the hearts showed a conspicuous and uniform enlargement with dilatation of all four chambers. Myocardial fibrosis was non-specific, and cellular infiltration was mild or absent. In nine of our initial 29 cases there was associated hepatic cirrhosis or fibrosis. There was also a high prevalence of the electrocardio-

graphic changes which are commonly associated with major or minor degrees of coronary insufficiency.

## Subsequent studies

Subsequent epidemiological studies of population samples in Jamaica showed an unexpectedly large number of relatively symptomless subjects with electrocardiographic signs usually considered characteristic of ischaemic heart disease (Fodor *et al.*, 1964). These surveys of two communities, one in a rural and the other in a suburban area, showed a higher prevalence of such electrocardiographic abnormalities than were found in similar surveys in the United States or Britain. We also found that cardiothoracic ratios calculated from anteroposterior chest radiographs were higher in Jamaica than in Wales (Stuart *et al.*, 1962; Ashcroft and Miall, 1969). These findings are difficult to explain in a community in which coronary atheroma and myocardial infarction are known to be uncommon (Robertson, 1959). Their frequent association, however, with symptoms of mild angina suggested not only a high community prevalence of an unusual form of heart disease but also that

these might be early examples of the disorder characterized in later life by unexplained cardiomegaly, congestive heart failure, and often sudden death.

Other studies in Jamaica showed the not uncommon association of idiopathic cardiomegaly with pregnancy, constituting the group usually known as peripartur or puerperal cardiomyopathy (Stuart, 1968).

Laboratory studies showed that there was no higher prevalence of heart antigens in these cardiomyopathies than was found in rheumatic, hypertensive, or other forms of acquired heart disease (Wilson and Stuart, 1970).

Coronary angiography during life confirmed that the major coronary vessels and their main branches were patent and of normal calibre. In at least two instances it was possible by this means to confirm a diagnosis of coronary ischaemia when this could not be differentiated from idiopathic cardiomegaly on clinical grounds. Necropsy coronary angiography was also performed in a number of subjects with idiopathic cardiomegaly, again demonstrating that the major coronary vessels were of normal calibre.

Long-term clinical, laboratory, and pathological study has now added significantly to our knowledge of this disorder. In this paper we review epidemiological and clinical aspects of patients with idiopathic cardiomegaly. We also give additional details of 46 patients who died during the past five years.

### Findings

**Epidemiological** Table 1 shows the prevalence of unexplained cardiomegaly on radiography in Jamaican male population samples in a rural and in an urban area. Selection was at random in the three decades between 35 and 64 years. All patients with cardiac enlargement were clinically examined. Unexplained cardiomegaly was defined as a cardiothoracic ratio exceeding 55 with blood pressures of less than 160 mm. Hg systolic or 95 mm. Hg diastolic, or both, and without significant cardiac murmurs on auscultation. The prevalence of unexplained cardiomegaly rises with age until it is 10 per cent in the rural and 7 per cent in the urban population samples in the 55-64 decade.

Table 2 shows an even higher prevalence in women, rising to 14 and 17 per cent in similar population samples in the 55-64 decade.

**Mortality statistics** Table 3 shows the mode of death in the 46 patients who died. In 11 (24%) death appeared to result solely

TABLE 1 *Prevalence of unexplained cardiomegaly in Jamaican population samples: men*

Age	No. radiographed	Rural		No. radiographed	Urban	
		Unexplained cardiomegaly No.	%		Unexplained cardiomegaly No.	%
35-44	69	5	7	90	1	1
45-54	73	8	11	77	3	4
55-64	73	7	10	41	3	7

TABLE 2 *Prevalence of unexplained cardiomegaly in Jamaican population samples: women*

Age	No. radiographed	Rural		No. radiographed	Urban	
		Unexplained cardiomegaly No.	%		Unexplained cardiomegaly No.	%
35-44	66	2	3	123	8	7
45-54	74	4	5	99	13	13
55-64	71	10	14	71	12	17

TABLE 3 *Mode of death in 46 patients with idiopathic cardiomegaly*

Mode of death	No.	%
Progressive cardiac failure	11	24
Sudden or unexpected	25	54
Unknown	10	22

from progressively refractive cardiac failure. It is this relatively small group, with its high morbidity and high hospital admission rate, which until recently provided most of our clinical and hospital experience of this disorder and accounted for our initial and probably false impression that the disorder was associated with an excessively high morbidity rate, that the course was progressive and inexorable, and that the prognosis after the development of heart failure was poor. Subsequent follow-up studies have shown that even after the initial onset of failure survival for 10 years or more without further decompensation was not uncommon.

In 25 of the 46 patients (54%) death was sudden or unexpected and not due to congestive failure, which when present had been reasonably well controlled. The importance of this group in the assessment of the mortality from this disorder cannot be overemphasized.

In 10 patients (22%) information about the mode of death was too inadequate for this to be classified accurately.

**Electrocardiographic findings** Table 4 analyses the electrocardiographic changes in 56 men and 62 women seen at the University Hospital in Jamaica with idiopathic cardiomegaly. There was a high rate of electrocardiographic abnormalities commonly regarded as characteristic of coronary artery disease (ST-T changes, QS complexes, and left bundle-branch block). One or other of these changes was found in 36 per cent of men and 40 per cent of women. Cardiac arrhythmias, particularly multiple ventricular extrasystoles, were common, and were found in 21 per cent of men and 24 per cent of women.

The classification of multiple ventricular extrasystoles was made when premature beats occurred on any one electrocardiographic tracing at more than five per minute. High voltage complexes considered characteristic of left ventricular hypertrophy were also common. These occurred in 42 per cent of men and 32 per cent of women.

Table 5 gives the electrocardiographic findings in relation to the mode of death in the 41 of the 46 patients in whom an electrocardiogram was available for study. It is seen that there is a high prevalence of arrhythmias, particularly ventricular extrasystoles, and that these ventricular extrasystoles were especially common in patients who had died suddenly or unexpectedly, having been present in 13 of the 23 patients (57%) so classified, and also in 5 of the 8 (63%) whose mode of death could not be determined.

**Clinical** High prevalence rates of electrocardiograms fulfilling the criteria for left ventricular hypertrophy are in keeping with the conspicuous left ventricular hypertrophy commonly seen clinically, and with the increased heart weights invariably found at necropsy.

Hearts enlarged to this extent on the basis of coronary artery disease do not normally show such high voltage potentials on electrocardiographic examination. These observations also confirm our impression that hypertrophy is the dominant lesion in these hearts and that wall-cavity ratios are high, and probably higher than those seen in congestive cardiomyopathy in other areas.

The electrocardiographic patterns commonly associated with ischaemic heart disease, the high prevalence of multiple ventricular extrasystoles, their common association with symptoms of mild angina and with the occur-

TABLE 4 *Electrocardiographic abnormalities in University Hospital patients with idiopathic cardiomegaly*

Electrocardiographic abnormalities	56 Men aged 21-64 years (mean 54 years)		62 Women aged 20-64 years (mean 51 years)	
	No.	%	No.	%
ST-T changes	9	16	9	15
QS complexes	5	9	5	8
Left bundle-branch block	6	11	17	27
Right bundle-branch block	10	18	4	6
Ventricular extrasystoles	12	21	15	24
Atrial fibrillation	9	16	7	11
Left ventricular hypertrophy	24	42	20	32

TABLE 5 *Electrocardiographic abnormalities in relation to mode of death*

Mode of death and No. of patients	Electrocardiographic abnormality						
	ST-T changes and QS items	Bundle-branch block	Left ventricular hypertrophy	Ventricular extra-systoles	%	Atrial fibrillation or other arrhythmia	
Progressive cardiac failure	10	3	4	3	1	10	3
Sudden	23	1	6	3	13	57	5
Unknown	8	1	5	1	5	63	2
Total	41	5	15	7	19	47	10

rence of sudden death, all suggested similarities with ischaemic heart disease occurring on a basis of major coronary artery disease.

Table 6 summarizes the similarities and differences between idiopathic cardiomegaly and coronary heart disease. The age at diagnosis is similar in both disorders except that idiopathic cardiomegaly is not uncommonly diagnosed in premenopausal women. It is of interest that of 13 women with idiopathic cardiomegaly below the age of 40 years, 11 (85%) were recognized because of unexplained congestive cardiac failure occurring soon after delivery and were classified as peripartal.

The onset of symptoms is usually sudden in coronary heart disease; it is slow and progressive in idiopathic cardiomegaly. Clinical cardiac enlargement is a late finding in the history of coronary heart disease, and the initial finding in patients with unexplained congestive failure. The prognosis after the heart is enlarged and after the onset of heart failure is usually poor in coronary heart

TABLE 6 *Comparison of coronary heart disease and idiopathic cardiomegaly in Jamaica*

	<i>Coronary heart disease</i>	<i>Idiopathic cardiomegaly</i>
Age group	Middle age and elderly	Similar, but not uncommon in premenopausal women
Onset	Usually sudden	Slow, progressive
Angina	Common: obtrusive	Common: mild
Clinical cardiac enlargement	Late finding	Initial finding
Prognosis after cardiac enlargement	Poor	Good
Prognosis after onset of cardiac failure	Poor	Good
Heart weight	Variable	Invariably increased
Left ventricular hypertrophy on electrocardiogram	Uncommon	Common
Conduction defects	Common	Common
Ventricular ectopics	Common	Common
Sudden death	Common	Common

disease, and commonly good in idiopathic cardiomegaly. Heart weight is variable in patients dying with coronary heart disease, but invariably increased in the idiopathic cardiomegalies. Electrocardiographic evidence of left ventricular hypertrophy is uncommon in coronary heart disease with or without cardiac enlargement. It is common in idiopathic cardiomegaly. Conduction defects, ventricular ectopic beats, and sudden death are common in both conditions.

**Lignocaine trial** It was the similarities with coronary heart disease and the suggestion that the majority of deaths might have been of dysrhythmic origin which suggested a line of approach to treatment and a possible means for reducing the mortality by suppressing the rates of emergence of fatal tachyarrhythmias, as has been achieved in coronary heart disease.

We have tested the effectiveness and duration of action of intramuscular lignocaine in reducing the number of ventricular extrasystoles. We thought that this would avoid many of the impracticalities of the intravenous route and produce a more sustained effect.

Scott and his colleagues (1968) have shown that intramuscular lignocaine can achieve plasma levels considered effective for the suppression of arrhythmias, and that these levels are quickly reached and may be maintained for a considerable period of time. The dose of choice seems to be 200 mg., which achieves adequate but not dangerously high serum levels of lignocaine.

The effects of intramuscular lignocaine in the first nine patients we studied are shown in Table 7. It is seen that this not only reduces considerably the number of ventricular extrasystoles but that this reduction can persist for several hours. These data suggest an approach to the treatment of the chronic ventricular

ectopic rhythms which characterize the cardiomyopathies, and possibly to the reduction of the high mortality rates with which they are associated. They may also be of value in other conditions characterized by ventricular arrhythmias, a striking example of which, of course, is acute myocardial infarction. Lown and Vassaux (1970), for instance, have recently suggested that 50 mg. lignocaine should be given intravenously to a patient with acute myocardial infarction immediately before transport to a hospital, and that this should be carried out even if no ectopic beats are detected. Our findings suggest that the intramuscular route, by its longer duration of action, may be a more effective method for preventing the emergence of ventricular arrhythmias during the period normally required for the transportation, examination, and admission of the coronary patient to hospital.

**Serological tests for treponemal infection** Fig. 1 compares the results of the Venereal Disease Research Laboratories test

TABLE 7 *Ventricular extrasystoles after intramuscular lignocaine*

Patient No.	1 hour before injection	Average No. of extrasystoles per minute			
		Hours after injection	½	2	4
1	10	2	3	—	—
2	12	0	0	—	—
3	7	1	2	—	—
4	8	1	2	—	—
5	5	2	2	—	—
6	5	0	0	—	—
7	6	1	0	—	—
8	8	2	1	—	—
9	11	6	2	1	4

for treponemal infection in the following categories of patients: (1) an urban population who have lived all their lives in the town and never in a rural area; (2) a group of patients who are attending our hypertensive clinic and who are considered characteristic of patients attending the outpatient clinics at the University Hospital; (3) patients from a rural area (Lawrence Tavern) where the transmission rate for yaws was known to have been high until recent years; and (4) the seventy-nine patients with cardiomyopathy (39 male and 40 female) in whom serological tests for treponemal infection were available.

Details of groups (1) and (2) are reproduced from the study of Ashcroft and co-workers (1967). There is a highly significant association of cardiomyopathy with a positive serology when compared with the urban group or the hypertensive outpatient population. Seropositive rates were also higher in the cardiomyopathies than in individuals from a selected rural area where high seropositive rates were known to occur.

This association does not necessarily establish an aetiological relationship with yaws or syphilis. However, studies to confirm and extend these observations are clearly indicated.

### Pathology

**Macroscopical appearances** Details of the pathology have been given in a recent paper (Campbell *et al.*, 1971). Gross cardiomegaly was present in the 21 cases studied at necropsy, the average heart weight being 675 g. Two hearts actually weighed more than a kilogram each. The characteristic globular appearance is seen in Fig. 2.

Dilatation and hypertrophy of all chambers was the rule. The myocardium was usually of normal consistency. In only two hearts was there easily discernible fibrosis in the gross specimen. Endocardial thickening was not a constant feature; it was mild and was usually limited to irregular mild fibrosis in the outflow tract. In four hearts small mural thrombi were seen in the apices of both ventricles.

The valves were in all cases within normal limits. The larger coronary vessels were free from atheromatous narrowing and in the majority of cases presented a normal picture when opened longitudinally. Coronary angiography was performed on 7 hearts. Fig. 3 is a typical result. The vessels showed a smooth outline with no evidence of occlusion or narrowing.

**Conduction system** The conduction system was examined carefully in serial sections

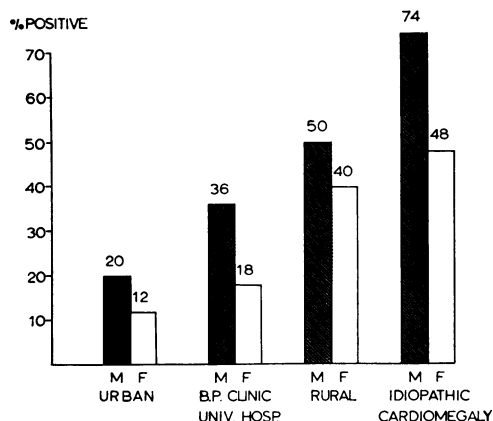


FIG. 1 Venereal Disease Research Laboratories tests in certain populations. See text.

because of the high prevalence of arrhythmias and conduction defects. The sinoatrial node showed an increase in fibrous tissue in these cases, though in none was there complete destruction. The atrioventricular node showed similar changes with some fibrosis in these hearts and haemorrhage and round-cell infiltrate in one.

FIG. 2 Globular-shaped heart weighing 1140 g.



The bundle of His showed changes similar to those seen in the atrioventricular node. The left bundle-branch was the site of widespread lesions in 13 of the 15 hearts. The right bundle showed patchy fibrosis in 4 cases, and necrosis in one.

**The intramuscular coronary arteries** In 3 of the hearts examined by serial sections it was noticed that many intramural vessels extending over several millimetres showed thickening of their walls. There was consequently a narrowing of the lumen, very obvious in some instances. The nature of this lesion is fully described in our previous paper. Fig. 4 and 5 are illustrative.

It should perhaps be re-emphasized that these changes in the intramural vessels occurred without a concomitant lesion in the large coronary arteries.

Histological changes in the myocardium were usually absent or non-specific.

Japanese workers have recently described the occurrence of unexplained cardiac failure in patients who were found to have normal main coronary artery systems but with occlusive abnormalities in the intramuscular vessels between 80 and 500  $\mu\text{m}$ . in diameter (Donomae *et al.*, 1962). They suggested that the lesions in these vessels may lead to chronic cardiac failure without anginal pain or other symptoms. They further suggest that in Japan, with its low rate of coronary atherosclerosis, presumably because of a low fat diet, coronary arteriolar sclerosis could be an important cause of the silent type of coronary heart disease which is so common in that country. Our findings also suggest that in Jamaica, with its comparable low rate of atherosclerosis, sclerosis of the smaller coronary vessels may be the cause of a type of coronary heart disease presenting clinically as unexplained cardiac enlargement and cardiac failure.

The implication is strong that the background of some cases of idiopathic cardiomegaly may be myocardial ischaemia occurring at a gradual and insidious pace and probably diffusely involving a smaller category of coronary vessel.

Although it is unlikely that this would entirely explain the high prevalence of the cardiomyopathies in Jamaica, it may provide useful additional information about at least a number of these unusual cases. The high association with a positive serology may also provide an additional avenue for further study. Although there are still many gaps in our knowledge, our opportunities for prolonged and detailed clinical and epidemiological study

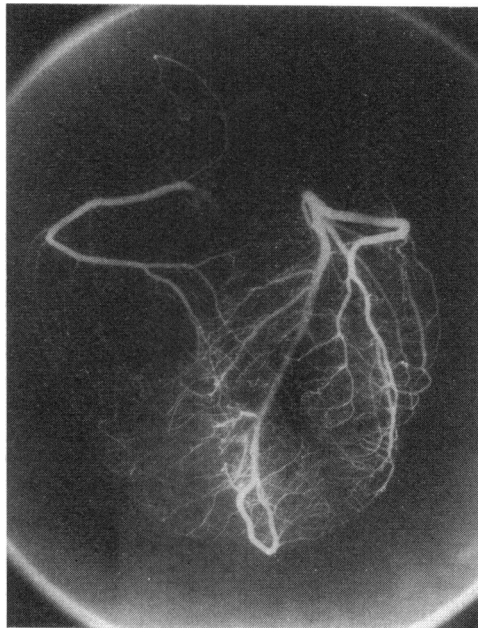
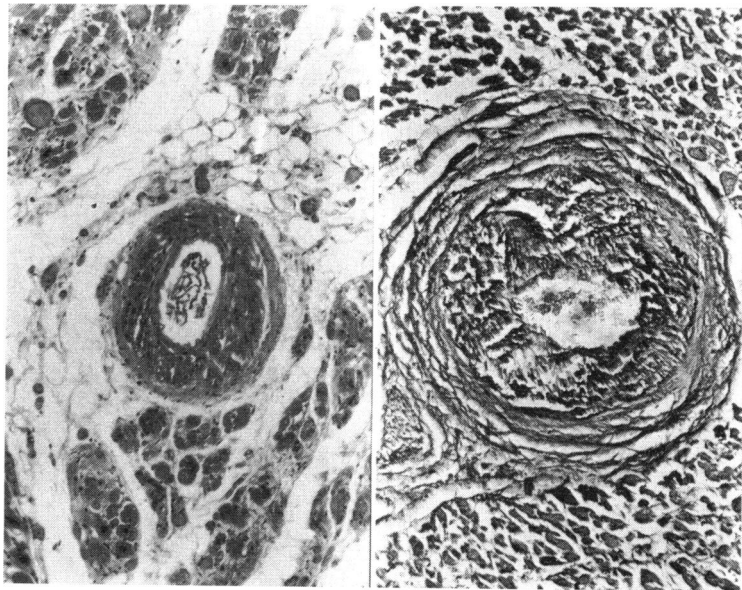


FIG. 3 An angiogram of the heart showing the smooth uniform coronary arteries.

FIG. 4 Thickening of the wall of a small blood vessel due mainly to medial hypertrophy. (H. and E.  $\times 200$ .)

FIG. 5 Thickening of the wall of an intramural blood vessel due mainly to intimal thickening. (Elastic van Gieson.  $\times 200$ .)



have already added significantly to our knowledge of this disorder particularly as seen in Jamaica and other West Indian territories.

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